

## REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. By this amendment, claims 34 and 35 are canceled, and claims 28, 36 and 44 have been amended to more clearly recite specific aspects of the instant invention. Support for the amendment may be found throughout the claims and specification as originally filed. Accordingly, no new matter has been added. This amendment is not to be construed as acquiescence to any rejection and is made without prejudice to prosecution of any subject matter modified by the amendment in a related divisional, continuation, or continuation-in-part application.

### Sequence Rule Compliance

The Action alleges that the application fails to comply with the requirements of 37 C.F.R. § 1.821-25, since Figures 1 and 7 recite sequences that are not accompanied by sequence identification numbers.

Applicants respectfully submit that sequence identifiers have been assigned to the sequences set forth in Figures 1 and 7, and the specification has been amended such that the Brief Description of the Figures now recites the SEQ ID NOs of these sequences. In addition, the Sequence Listing has been amended to include these additional SEQ ID NOs. The enclosed electronic and paper copies of the Sequence Listing include no new matter that goes beyond the original application as filed. Furthermore, the above amendments, which merely direct the insertion of the Sequence Listing and insertion of sequence identifiers, include no matter that goes beyond the original application as filed. Applicants respectfully submit that the above-identified application is now in compliance with 37 C.F.R. §§ 1.821-1.825 and WIPO Standard ST. 25.

Objections to the Claims

The Action objects to claims 36-39 as allegedly being essentially identical to claims 28-31. More specifically, the Action alleges that the claims are drawn to the same composition, since the language "consisting essentially of" in claims 36-39 is interpreted to mean the same as "comprising," as recited in claims 28-31.

Applicants respectfully submit that the scope of these claims is different. Nonetheless, without acquiescence to this basis of objection, claim 36 has been amended to remove the phrase "consisting essentially of" and to more clearly claim one specific embodiment of the invention. Accordingly, Applicants respectfully request that this basis of objection be withdrawn.

The Action objects to claims 28-31, 36-39, and 44-47 on the basis that SEQ ID NO:1, which is referred to in these claims as an amino acid sequence, is a polynucleotide sequence in the sequence listing.

Applicants respectfully submit that SEQ ID NO:1 contains both a polynucleotide sequence and its encoded polypeptide sequence. However, for the purpose of providing additional clarity, Applicants submit with this amendment a substitute sequence listing, which provides the separate sequence identifier, SEQ ID NO:19, for the polypeptide sequence set forth in SEQ ID NO:1. Claims 28, 36, and 44 have been amended to refer to SEQ ID NO:19. Applicants further submit that SEQ ID NO:19 does not constitute new matter, since the sequence was provided in SEQ ID NO:1 in the application as filed. Applicants respectfully request that this basis of objection be reconsidered and withdrawn.

The Action objects to claims 28-31, 36-39, and 44-47, alleging that the language referring to functional variants and functional equivalents is not clear. Similarly, the Action objects to the same claims on the alleged basis that the word "derived" is unclear in the context of the claims. Applicants note that the claims have been amended to delete reference to functional variants and functional equivalents and to remove the word "derived," thereby

obviating the basis of these objections. Applicants, therefore, request that the objections be withdrawn.

The Action also finds the oath or declaration to be defective, since the residence is allegedly not provided as required under 37 C.F.R. § 1.52(c). Applicants submit that the declaration fully complies with 37 C.F.R. § 1.63 and, thus, 37 C.F.R. § 1.52(c). Applicants note that Applicant's place of residence is not required in the oath or declaration, if it is included in an application data sheet (See M.P.E.P. § 605.02 and 37 C.F.R. § 1.76). Applicants further submit that Applicants' residences are provided in the application data sheet filed February 19, 2002. Applicants respectfully request that this basis of rejection be reconsidered and withdrawn.

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Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 28-31, 36-39, and 44-47 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicants had possession of the claimed invention at the time of filing. More specifically, the Action alleges that the specification fails to provide sufficient guidance regarding common structural and functional attributes of Smac fragments and variants to support the claimed genus.

Applicants respectfully traverse this rejection and submit that the instant application clearly conveys to the skilled artisan that Applicants had possession of the claimed invention at the time of filing. Applicants further submit that the instant specification provides adequate written description to support the genus of claimed polypeptide fragments and variants. Under the Examination Guidelines set forth by the Patent and Trademark Office, the written description requirement for a claimed genus may be satisfied by the description of a representative number of species or the disclosure of relevant, identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099, at 1106. Applicants submit that the instant application

discloses sufficient relevant, identifying characteristics to show that Applicants were in possession of the claimed genus of polypeptide fragments and variants.

Applicants submit that the specification describes the identification of two regions of the Smac polypeptide capable of binding to domains of IAP and promoting caspase activity. These two regions include an NH<sub>2</sub>-terminal region, which binds to the BIR3 domain and promotes caspase-9 activity, and an internal region including a portion of amino acid residues 22-139 of the Smac polypeptide, which binds to the BIR1 and/or BIR2 domain and promotes caspase-3 and caspase-7 activity. Furthermore, Applicants have demonstrated that the seven NH<sub>2</sub>-terminal residues of the mature Smac polypeptide are sufficient for binding to IAP and activating caspase-9. Accordingly, Applicants submit that they have disclosed both structural and functional characteristics of the claimed polypeptides, including specific amino acid residues and the functional attributes of binding to IAP BIR domains and promoting caspase activity. Based upon these detailed structural and functional characteristics, Applicants submit that the skilled artisan would recognize that Applicants were in possession of the claimed genus of polypeptides, including structural variants possessing these characteristics.

Nonetheless, without acquiescence to this basis of rejection and solely to expedite prosecution of the instant application, claims 28, 36 and 44 have been amended to remove reference to functional variants and functional equivalents. In addition, claim 28 has been amended to be directed to polypeptides comprising at least residues 56-62 of SEQ ID NO:19, and claims 36 and 44 have been amended to be directed to polypeptides comprising or consisting of at least seven contiguous residues of amino acids 56-139 of SEQ ID NO:19, respectively. Support for these amendments is provided throughout the specification as originally filed. Specifically, support for claim 28 is provided on page 44, lines 22-24, and support for claims 36 and 44 is provided on page 17, line 18, through page 18, line 3. In light of these amendments and remarks, Applicants submit that the instant application provides adequate written description of the claimed invention and respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 28-31, 36-39, and 44-47 stand rejected under 35 U.S.C. § 112, first paragraph, on the alleged basis that the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with the claims. More specifically, the Action alleges that the specification, while being enabling for a peptide or polypeptide consisting of at least the first seven amino acids of residues 56-139 of the Smac polypeptide, does not provide reasonable enablement for a peptide or polypeptide having at least any two contiguous amino acid residues of residues 56-139 of the Smac polypeptide, or functional variants or equivalents thereof, that bind to BIR1 and BIR2.

Applicants traverse this basis of rejection and respectfully submit that the skilled artisan, based upon the instant specification and further in light of the general knowledge in the art, would be enabled to practice the full scope of the claimed invention. As described above, the instant specification teaches the skilled artisan of two functional domains within the Smac polypeptide, both of which are capable of binding to IAP and promoting caspase activity. Further, the specification teaches specific residues associated with these functional domains. For example, the specification teaches that the first seven residues of mature Smac are sufficient for these activities and that a second region requiring at least a portion of residues 22-139 also possesses these activities. Applicants submit that the skilled artisan, apprised of these functional domains and their associated activities by the instant application, could readily make and use Smac polypeptides and variants thereof of the invention. Applicants submit that methods of producing polypeptides of a given sequence and variants thereof are widely known and routine in the art. Furthermore, methods of screening variants for their ability to bind to IAP or a BIR domain thereof are also considered merely routine in the art, particularly in light of the guidance provided by the instant specification, which described methods of determining whether a polypeptide binds to IAP or a BIR domain thereof, and whether a polypeptide promotes caspase activity (See, e.g., Examples 2 and 3). Accordingly, Applicants submit that the skilled artisan could readily ascertain whether any particular Smac polypeptide or variant thereof possessed the

recited functional characteristic of binding to at least a portion of an IAP using routine procedures and without undue experimentation.

Nonetheless, without acquiescence to this basis of rejection and solely to expedite prosecution of the instant application, claims 28, 36 and 44 have been amended to remove reference to functional variants and functional equivalents. In addition, claim 28 has been amended to be directed to polypeptides comprising at least residues 56-62 of SEQ ID NO:19, and claims 36 and 44 have been amended to be directed to polypeptides comprising or consisting of at least seven contiguous residues of amino acids 56-139 of SEQ ID NO:19, respectively. Applicants submit that the skilled artisan could readily make and use polypeptides comprising seven contiguous amino acid residues of Smac, which bind at least a portion of an IAP. Indeed, the Action acknowledged that Smac polypeptides comprising the first seven residues are enabled by the instant specification (page 9, lines 3-6). Applicants submit that the instant application also provides adequate disclosure to enable the skilled artisan to make and use any Smac polypeptide comprising at least seven residues of amino acids 56-139, which binds at least a portion of an IAP polypeptide, since the specification provides routine screening methods for determining the ability of a polypeptide to bind to a region of IAP. Accordingly, Applicants submit that the claims are fully enabled and respectfully request that this rejection in reconsidered in light of these amendments and remarks.

Rejection Under 35 U.S.C. § 102(b)

Claims 28, 36, and 44 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Heilig *et al.* Specifically, the Action asserts that Heilig *et al.* teaches an amino acid sequence comprising the amino acids ALA-VAL, although the Action concedes that the reference does not teach that the polypeptide is capable of binding to the BIR domains BIR1 and BIR2.

Applicants respectfully traverse this basis of rejection. As an initial matter, Applicants note that Heilig *et al.* is a Genbank Sequence Database listing (Accession S02013), and, therefore, Applicants believe that the intended basis of this rejection is 35 U.S.C. § 102(b).

In addition, Applicants submit that the claims have been amended to recite polypeptides comprising at least seven contiguous residues of amino acids 56-139 of the Smac polypeptide, without acquiescence to this basis of rejection. Since Heilig *et al.* fail to disclose a polypeptide comprising at least seven contiguous residues of amino acids 56-139 of the Smac polypeptide, this basis of rejection is obviated by the claim amendments, and Applicants respectfully request that this basis of rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(e)

Claims 28, 36, and 44 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,110,691 (the '691 patent). More specifically, the Action alleges that the reference teaches a Smac polypeptide of SEQ ID NO:1 (amino acid residues 1-239), although the Action concedes that the reference does not teach that the Smac polypeptide is capable of specifically binding to the BIR domains BIR1 and BIR2.

Applicants traverse this basis of rejection and submit that the references fails to anticipate the claimed invention, which is directed to functional fragments of the Smac polypeptide, and variants thereof, which bind to at least a portion of an IAP polypeptide. Applicants submit that the '691 patent fails to teach or suggest any fragment of the Smac polypeptide that is capable of binding to at least a region of an IAP. Indeed, the '691 patent does not even disclose or recognize that Smac polypeptides bind IAP. Applicants note that claims 28, 36 and 44 have been amended to recite polypeptides having up to 183 contiguous residues of mature Smac, thus excluding full length mature Smac polypeptides. Support for this amendment may be found, for example, on page 17, lines 13-25. Accordingly, Applicants respectfully submit that this reference does not describe the claimed invention and, thus, cannot anticipate the claimed invention. Applicants respectfully request that this basis of rejection be withdrawn.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

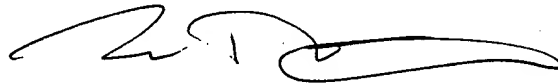
Application No. 09/939,293  
Reply to Office Action dated February 27, 2003

All of the claims remaining in the application are now believed allowable.  
Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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